

# Respiratory Failure in the Course of Treatment of Diabetic Ketoacidosis

Anil Regmi, MD, Nikifor K. Konstantinov, Emmanuel I. Agaba, MBBS, Mark Rohrscheib, MD, Richard I. Dorin, MD, and Antonios H. Tzamaloukas, MD

## PRESENTATION

Three patients developed acute respiratory failure during treatment of diabetic ketoacidosis (DKA) diagnosed by the combination of hyperglycemia, anion gap metabolic acidosis, and presence of ketone bodies in serum. All three required tracheal intubation and mechanical ventilation.

Table 1 shows pertinent laboratory values at admission and immediately before tracheal intubation. Serum anion gap was computed as  $[\text{Na}]_s - ([\text{Cl}]_s + [\text{TCO}_2]_s)$ , where  $[\text{Na}]_s$ ,  $[\text{Cl}]_s$ , and  $[\text{TCO}_2]_s$  are, respectively, the serum sodium, chloride, and total carbon dioxide concentrations. Serum tonicity in mOsm/l was calculated as  $2 \times [\text{Na}]_s + [\text{Glu}]_s$ , where  $[\text{Glu}]_s$  is serum glucose concentration in mmol/l.

### Patient 1

A 12-year-old girl with no previous history of diabetes was admitted with DKA, symptomatic hypovolemia, and lethargy. On admission, her serum potassium concentration was in the normal range (Table 1), and her serum phosphate was 6.1 mg/dl.

Initial treatment consisted of infusion of insulin and large volumes of saline. After 4 hours, she experienced cardio-respiratory arrest. Electrocardiogram showed ventricular fibrillation. Laboratory values obtained just before the arrest revealed profound hypokalemia and hypercapnia (Table 1).

She recovered after electro-mechanical resuscitation, intubation, and infusion of large amounts of potassium chloride. However, she developed acute kidney injury, which improved without the need for dialysis and required prolonged tracheal intubation (1 week).

### Patient 2

A 14-year-old boy with no history of diabetes was admitted with DKA, coma, seizures, and profound hypotension. Computed tomography did not reveal any brain pathology. Admission laboratory values showed extreme hyperglycemia with hypertonicity and hypokalemia (Table 1).

The boy received intravenous insulin plus large volumes of saline containing potassium chloride. After 3 hours, his hypotension had improved, but his serum glucose level was 1,794 mg/dl, serum sodium was 148 mEq/l, serum tonicity was 391.7 mOsm/l, serum chloride was 112 mEq/l, total serum carbon dioxide was 9 mmol/l, serum anion gap was 27 mEq/l, and serum potassium was 3.3 mEq/l. The rate of saline infusion was decreased. Potassium concentration in the infusate was increased by adding potassium phosphate, but the overall rate of potassium infusion was decreased, while the patient's urine output increased substantially. The patient's hypokalemia subsequently worsened, and he developed hypercapnia (Table 1), leading to intubation. His

serum phosphate was 2.5 mg/dl just before intubation.

Infusion of insulin, hypotonic saline, and potassium salts led to correction of all of his biochemical abnormalities. He remained intubated for 5 days and had prolonged confusion, followed by severe depression. He required a hospitalization of 25 days.

### Patient 3

A 35-year-old woman with type 1 diabetes and no known pulmonary disease was admitted with symptoms of upper respiratory infection, DKA, hypotension, and confusion. Four days before admission, she withheld her insulin because of poor food intake. On admission, lung examination and chest X-ray were unremarkable. Initial laboratory values showed inadequate respiratory compensation for the metabolic acidosis (Table 1). In addition, her serum phosphate level was 5.8 mg/dl.

She received an infusion of insulin and large volumes of saline containing potassium chloride. She experienced progressive dyspnea and had a respiratory arrest 6 hours after initiation of treatment. Just before the arrest, serum chemistries had improved (Table 1). She was intubated and ventilated mechanically. Repeated chest X-rays revealed extensive bilateral lung infiltrates. Pneumococcal pneumonia was diagnosed by sputum and blood cultures.

She was treated with ampicillin sulbactam plus gentamicin and had

**Table 1. Laboratory Values on Admission and Immediately Before Tracheal Intubation**

Laboratory Value	Patient 1		Patient 2		Patient 3	
	On Admission	Before Intubation	On Admission	Before Intubation	On Admission	Before Intubation
Serum glucose (mg/dl)	790	203	2226	1273	824	325
Serum glucose (mmol/l)	43.9	11.1	123.7	70.7	45.8	18.1
Serum sodium (mEq/l)	132	144	135	159	136	140
Calculated serum tonicity (mOsm/l)	307.9	299.3	393.7	388.7	317.8	298.1
Calculated serum osmolarity* (mOsm/l)	322.2	308.2	419.1	409.7	334.2	306.0
Serum chloride (mEq/l)	91	108	94	128	97	111
Serum total carbon dioxide (mmol/l)	5	21	9	13	10	16
Calculated serum anion gap (mEq/l)	36	15	32	18	29	13
Serum potassium (mEq/l)	3.8	1.1	2.4	2.1	6.0	3.9
Arterial blood pH	7.02	7.09	7.209	7.136	6.99	—
Arterial blood PaO <sub>2</sub> (mmHg)	102†	48†	226‡	177‡	58§	—
Arterial blood PaCO <sub>2</sub> (mmHg)	18	68	16	48.9	39	—
Expected range of PaCO <sub>2</sub>    (mmHg)	10–18	34–42	13–21	29–37	18–26	—
Arterial blood bicarbonate (mEq/l)	4.6	20.1	6.2	16.1	9.4	—

\*Osmolarity was calculated by the formula 2 serum sodium + serum glucose in mmol/l + serum urea in mmol/l.

†Room air, sea level.

‡6 L/min of oxygen by phase mask, 1,500 m altitude.

§Room air, 1,500 m altitude.

||The expected range of PaCO<sub>2</sub> was calculated from the arterial blood bicarbonate concentration using the Fulop formula.<sup>17</sup>

a slow recovery. She remained intubated for 6 days.

**QUESTIONS**

1. What were the mechanisms of respiratory failure in these cases?
2. What measures could have prevented respiratory failure during the course of treatment of DKA?

**COMMENTARY**

The development of respiratory failure in these patients was heralded by specific laboratory findings that were not addressed early in the course of treatment. Respiratory failure developed because of severe hypokalemia in the first two patients and after hydration led to rapid development of

extensive pneumonic infiltrates in the third patient.

Both external and internal potassium balances are disturbed during the development and treatment of DKA. Glycosuria leads to urinary losses of potassium through osmotic diuresis.<sup>1</sup> Potassium losses occurring both before and during treatment of DKA must be replaced. The required potassium replacement varies greatly.<sup>2</sup> The evaluation of potassium deficits is complicated by potassium exit from cells into the extracellular compartment and hyperkalemia because of absence of insulin, hypertonicity, and probably DKA itself.<sup>3,4</sup>

The interplay of the influences on internal and external potassium balances in DKA leads to a wide variation of presenting serum potassium levels, which are usually elevated or in the normal range. Hypokalemia at presentation is seen in ~ 5% of cases.<sup>2</sup> Hypokalemia or even a normal potassium level in DKA are signs of profound potassium deficits.<sup>5</sup> Infusion of potassium salts before infusion of insulin and saline is recommended in such instances,<sup>6</sup> because of an anticipated drop in serum potassium during treatment.

Insulin administration tends to reverse all influences that caused exit of potassium from the cells.<sup>4</sup>

The magnitude of cellular potassium uptake during treatment of DKA cannot be predicted accurately. Extracellular volume expansion through infusion of large volumes of saline and, more importantly, ongoing urinary losses of potassium as long as glycosuria persists have additional hypokalemic effects. Therefore, serum potassium should be monitored frequently during treatment of DKA.

The combination of potassium deficits and the hypokalemic effects of treatment may cause respiratory failure reversible with intubation and potassium infusion.<sup>7,8</sup> The first two cases reported here illustrate this sequence. The treatment issue with the first patient, who presented with a “normal” potassium level, was omission of administration of potassium from the onset of treatment. In the second patient, a reduction in the rate of potassium infusion was coupled with both a large increase in urine volume (and probably in urinary potassium losses as circulatory status recovered and the serum glucose level was still very high) and continuous insulin-mediated cellular uptake of potassium. This combination caused a drop in potassium and respiratory failure. In patients with DKA and initially low or normal potassium levels, urinary potassium losses should be monitored during treatment and should be used, along with monitored serum potassium values, as guides to potassium infusion.

When addressing potassium metabolism in DKA, two other issues should be considered: 1) potassium deficits may be refractory to potassium replacement in patients with severe magnesium deficits,<sup>9</sup> and 2) potassium deficits may cause life-threatening cardiac complications in addition to respiratory failure.<sup>10</sup> Monitoring serum potassium is the best way to prevent these compli-

cations. Mechanisms other than potassium disorders that may cause respiratory failure at presentation or during treatment of DKA include phosphate deficit,<sup>11</sup> acute respiratory distress syndrome,<sup>12</sup> cardiac pulmonary edema in patients with renal failure who develop extracellular expansion from osmotic shift of intracellular water into the extracellular compartment during severe hyperglycemic episodes,<sup>13</sup> and respiratory complications of cerebral edema<sup>14</sup> and peripheral neuropathies.<sup>15</sup>

The third case reported here illustrates another mechanism of the development of respiratory failure in DKA. Profound volume deficits may mask the radiographic features of pneumonia in patients with DKA and may cause delays in the diagnosis of pneumonia. Pulmonary infiltrates blossom after hydration in these patients and may cause respiratory failure. The clue to the presence of pulmonary pathology on admission of this third patient was an inadequate respiratory response to the metabolic acidosis.

Albert et al.<sup>16</sup> calculated a tight correlation (0.97) between plasma bicarbonate from arterial blood gases ( $[HCO_3]_p$ ) and the partial pressure of arterial carbon dioxide ( $PaCO_2$ ) in patients with simple metabolic acidosis. Fulop’s analysis<sup>17</sup> of 27 episodes of DKA without any other acid-base abnormality revealed the following formula, which is similar to the formula developed by Albert et al.:  $PaCO_2 = 7.27 \times (1.57 [HCO_3]_p) \pm 4.04$  mmHg.

Deviations of the respiratory response in patients with DKA call for a search for respiratory pathology, central nervous system pathology, or peripheral neuromuscular pathology. In the third patient, such a search could have led to early treatment of the pneumonia and

prevented or attenuated the respiratory failure.

### CLINICAL PEARLS

- Replacement of potassium deficits is a primary aim of the treatment of DKA. Serum potassium levels and, in selected cases, urinary potassium losses should be monitored and used as the guide to potassium replacement.
- The respiratory response to the degree of metabolic acidosis should be evaluated at presentation and, in selected cases, during treatment of DKA. Any deviation of this response outside the expected range should lead to a systematic search for its mechanism.

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*Anil Regmi, MD, is a fellow in the Division of Nephrology; Nikifor K. Konstantinov is a medical student; Mark Rohrscheib, MD, is an associate professor of medicine in the Division of Nephrology; and Richard I. Dorin,*

*MD, is a professor of medicine in the Division of Endocrinology at the University of New Mexico School of Medicine in Albuquerque. Antonios H. Tzamaloukas, MD, is an emeritus professor of medicine at the University of New Mexico School of Medicine and a nephrologist at the Raymond G. Murphy Veterans Affairs Medical Center in Albuquerque. Emmanuel I. Agaba, MBBS, is an associate professor of medicine in the Division of Nephrology at the Jos University School of Medicine in Jos, Plateau State, Nigeria.*